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Breast-Conserving Surgery for Invasive Cancer: A Principle Based on Segmental Anatomy

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As the incidence of breast cancer increases in Japan, breast-conserving surgery becomes an important issue in the light of quality of life. We have demonstrated by 3-D reconstruction studies that ductal carcinoma in situ (DCIS) originates from the terminal duct-lobular unit (TDLU). Normal mammary epithelium anatomically located in the TDLU was shown to be biologically associated with cancerous change, particularly in specimens from patients who subsequently developed invasive carcinoma. Atypical ductal hyperplasia as well as DCIS expressed breast cancer associated antigen, providing further biological evidence that the atypical lesion at the TDLU are premalignant. Intraductal spread of carcinoma was defined as “DCIS was present clearly extending beyond the TDLU, or present prominently within the large ducts,” and was classified into 3 grades according to the distribution of carcinoma in the duct-lobular system. We have developed a breast-conserving surgery consisting of quadrantectomy and regional lymph node dissection and immediate volume replacement using lateral tissue-flap (LTF). The quadrantectomy was employed on the basis of segmental anatomy of the ductlobular system in which breast carcinoma originates. Fairly good cosmetic outcome as well as local control were obtained in the patients who underwent the immediate volume replacement using LTF. It must be emphasized that the quadrantectomy is a radical procedure in the sense that it aims at removal of all the carcinoma cells of the primary tumor.

Key words--- breast cancer; breast-conservative surgery; ductal carcinoma in situ; intraductal spread of carcinoma; quadrantectomy

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Dr. N. Ohuchi is a recipient of the 1998 Gold Prize, Tohoku University School of Medicine.
Effect of Mandibular Advancement Splint on Psycho-Intellectual Derangements in Patients with Sleep Apnea Syndrome

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- The mandibular advancement splint (MAS) was recently introduced for the management of sleep apnea syndrome (SAS), although its effects on psycho-intellectual functions have not been elucidated yet. We examined psycho-intellectual function before and after treatment with MAS in patients with SAS. Twenty patients with SAS underwent psycho-intellectual function testing before and after treatment with MAS for 3 to 4 weeks. The apnea index significantly decreased from 19.0±15.6 to 2.4±1.9. The state anxiety score significantly decreased from 44.6±12.1 to 33.7±11.1, the trait anxiety score significantly decreased from 46.2±13.4 to 37.6±13.8, and the depression scale score significantly decreased from 39.2±11.0 to 30.8±9.9 with MAS treatment. By the Cornell Medical Index and the Yatabe-Guilford test, the patients became less neurotic and less eccentric after treatment. By the Uchida-Kraepelin psychodiagnostic test, calculation ability significantly increased from 1247.4±402.1 to 1950.2±651.9. We conclude that MAS treatment reduces apneic episodes and improves psycho-intellectual derangements in patients with SAS.

Key words--- sleep apnea syndrome; mandibular advancement splint; nocturnal desaturation; psycho-intellectual function

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Creatinine at the Evaluation of Urinary 1-Methyladenosine and Pseudouridine Excretion

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- The elevation of urinary modified nucleosides levels in urine is found in patients with cancers. In the present study, we have tested 616 urine samples randomly collected from non-malignant cases. Thirty-two percent (194/616) and 11% (68/616) had elevated levels of 1-methyladenosine and pseudouridine, respectively (They are designated as false-positive cases). To elucidate the cause on non-specific elevation of the nucleosides, the correlation between creatinine excretion level and urinary nucleosides levels were determined. The result revealed that false-positive cases were frequently detected in patients with lower creatinine excretion levels. The mean creatinine levels of false-positive cases were significantly lower than those of negative cases. From these results, the false-positive of urinary 1-methyladenosine and pseudouridine might be due to the low creatinine excretion mainly caused by the renal dysfunction. Creatinine excretion in each individual should be taken into consideration in case of determining urinary modified nucleosides.

Key words--- modified nucleosides; 1-methyladenosine; pseudouridine; creatinine excretion
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Determing Factors of Mortality in the Elderly with Hip Fractures

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We conducted a retrospective study of the influence of various factors on the mortality of 114 patients with hip fractures. The mortality rate one year after surgery was 18%, which was 2.5 times larger than that of the general population. It was related to age, ECG abnormality, and post-operative complications.

Key words--- hip fractures; femoral neck fractures; mortality; one-year survival

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Correlation between Magnetic Resonance Imaging and Clinical Profiles of Periventricular Leukomalacia

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- Magnetic resonance imaging (MRI) findings of 70 children with periventricular leukomalacia (PVL), examined between 1 year 2 months and 8 years of age (mean: 2 years 4 months of age), were analysed. Neurological assessments were made between 1 year 3 months and 15 years (mean: 4 years 9 months). The possible correlations between MRI findings and clinical profiles of PVL were investigated using three parameters of the MRI findings. The grade of ventriculomegaly correlated well with the severity of cerebral palsy (CP) but not with the severity of mental impairment. The grade of reduction of periventricular white matter correlated well with the severity of CP and mental impairment, and is the most reliable parameter for neurological prognosis. The degree of periventricular hyperintensity on T2-weighted images did not correlate well with severity of CP, but correlated to some degree with mental impairment. There was a significantly lower degree of periventricular hyperintensity in children at less than 28 weeks of gestation than at 28 or more weeks of gestation, but no significant difference in other parameters. The periventricular hyperintensity should be evaluated in view of the gestational age.

Key words—periventricular leukomalacia; magnetic resonance imaging; preterm infant; cerebral palsy; mental retardation

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Escape of Parasympathetic Vasodilatation from Sympathetic Attenuation in Oro-Facial Areas in the Cat

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We examined the effects of concurrent repetitive stimulation of the cervical sympathetic trunk (CST) on the parasympathetically mediated reflex blood flow increase in the orofacial area of cats. In urethane plus α-chloralose anaesthetized cats, parasympathetic reflex vasodilatation in the ipsilateral lower lip was elicited by electrical stimulation of the central cut end of the lingual nerve (LN). This blood flow increase was attenuated in a frequency-dependent manner when CST was stimulated concurrently at 0.5-10 Hz for 10 minutes. When we applied repeated LN stimulation (using identical parameters, each time) at intervals during a 30-minutes period of 10 Hz CST stimulation, the attenuation of the blood flow increase gradually weakened in a time-dependent manner even though the direct vasoconstrictor effect of CST stimulation showed no such decline.

Key words--- parasympathetic reflex vasodilatation; sympathetic-attenuation; orofacial; cat

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The Effects of Tone Exposure on the Inner Ear Functions in the Guinea Pig: Impact Tone vs. Steady State Tone

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- The damage-risk criterion (DRC) for hearing supposes that sound exposure with equal energy implies equal risk for noise-induced hearing loss (NIHL). We measured cochlear microphonics (CM), compound action potential (CAP), endocochlear potential (EP) and K⁺ ion concentration in the scala media, to see if the same level of $Leq_{24h}$ (impact tone and steady state tone) induced the same physiological changes in the inner ear function or not. Regarding the equal energy principle (EEP), we also examined if the EEP is appropriate or not at exposure of moderate level tone. We also checked how the time interval between impact tones affects or not the inner ear functions at the same $Leq_{24h}$ tone exposure. Therefore we used exposure at 1 pulse/second or 1 pulse/3 seconds and steady state tone exposure at $Leq_{24h}=90, 85$ and $80$ dB. The results are the following.

Both steady state and impact tone exposure causes change of the electrophysiological data. First, CM maximum output voltage after exposure to impact tone of 115 dB ($Leq_{24h}=90$ dB) was lower than after exposure to a 8 kHz steady state tone of 90 dB. CAP threshold (below 10 μV) obtained after the 115 and 110 dB exposure of impact tone were 5-10 dB higher than that of steady state tone of 90 dB. The negative EP induced by impact tone exposures showed the same tendency as the CM experiments. Having more frequent pulses (1 pulse/second vs. to 1 pulse/3 seconds) showed more inhibition. The K⁺ concentration time course remained similar to the control when the $Leq_{24h}$ was low (80 dB). Impact tone exposure induced stronger effects to the inner ear at exposure of moderate level tone than that of steady state tone of $Leq_{24h}$.

**Key words**--- impact tone exposure; equal energy principle; CM; CAP; EP; K⁺ ion

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Noncardiogenic Pulmonary Edema as the Chief Manifestation of a Pheochromocytoma: A Case Report of MEN 2A with Pedigree Analysis of the RET Proto-Oncogene

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Pheochromocytomas are rare neoplasias of the adrenal medulla which generally present with paroxysmal or sustained hypertension. Cardiogenic pulmonary edema is a common feature of these tumors, but few cases have been described with noncardiogenic pulmonary edema. We report a pheochromocytoma with the principle manifestation of noncardiogenic pulmonary edema and characterize a genetic lesion associated with the disorder. A 30-year-old man was admitted with abdominal pain and breathlessness. X-Ray examination of the chest revealed a massive, diffuse infiltration of the left lung without cardiomegaly. No paroxysmal blood pressure fluctuations or heart failure were evident during the entire course, and the infiltrate and dyspnea resolved in three days without inotropic or diuretic agents. Serum norepinephrine and epinephrine levels were elevated twenty and fifty times above normal, respectively. The patient was ultimately diagnosed with multiple endocrine neoplasia type 2A (MEN 2A). Mutations in the RET proto-oncogene have been described recently in patients with MEN 2A. Mutation analysis of selected RET exonic sequences identified a germline mutation at codon 634 in exon 11 of the RET proto-oncogene. The mutation introduces a transition encoding a non-conservative substitution from TGC (Cys) to CGC (Arg) and creates a novel restriction site recognized by HhaI. We further screened for this mutation among four of the proband’s relatives by HhaI restriction analysis. One asymptomatic family member was identified who subsequently elected prophylactic total thyroid removal. Histological examination of this specimen confirmed the presence of medullary thyroid carcinoma.

Key words--- pheochromocytoma; noncardiogenic pulmonary edema; multiple endocrine neoplasia type 2A; RET proto-oncogene; presymptomatic diagnosis

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